MEMORANDUM

10-August-2001

SUBJECT: **Diuron.** Results of the Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Meeting Held on 03-JULY-2001.

Reregistration Case No.: 0046
PC Code: 035505
DP Barcode No.: D275688

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THROUGH: Alan Nielsen, Branch Senior Scientist
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Christine Olinger, MARC Chair
Health Effects Division [7509C]

TO: Yan W. Donovan, MARC Executive Secretary
Health Effects Division [7509C]

1. Attendance

MARC Members:

Alberto Protzel, Richard Loranger, Yan Donovan, Sheila Piper, Abdallah Khasawinah, Christine Olinger, David Nixon.

Non members attended:

Rich Griffin, Ibrahim Abdel-Saheb, James Jim Breithaupt, Sherrie Kinard, Carol Christensen, Diana Locke, John Punzi.

MARC Members Absent:

William Wassell.

MARC Members Absent but providing comments:

John Doherty

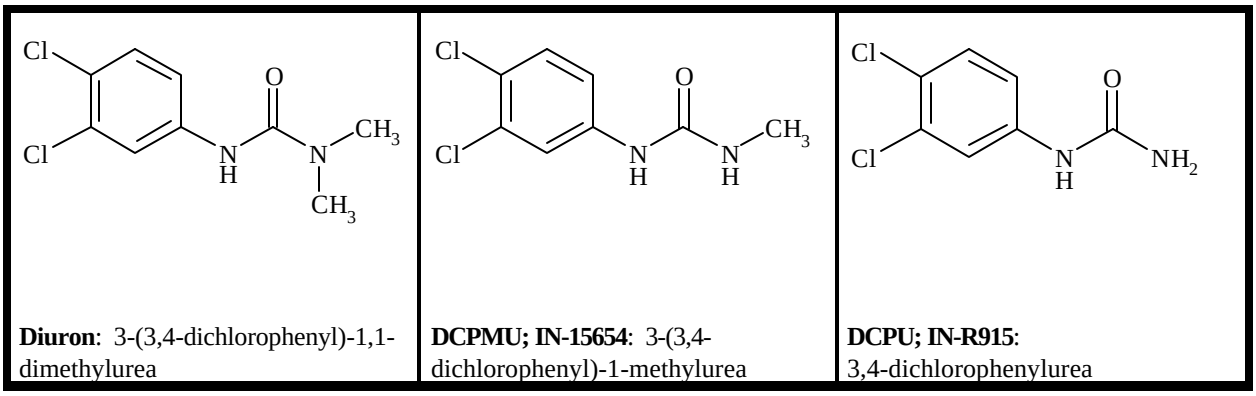
2. Summary of Deliberations

The metabolism of diuron in plants and animals from results of wheat, corn, orange, ruminant, and poultry studies together with the environmental fate studies conducted for diuron was presented to the HED MARC on 03/July/2001.

The ^{14}C-containing residues that were identified in oranges were: diuron, 3,4-dichlorophenylurea (DCPU), and 3-(3,4-dichlorophenyl)-1-methylurea (DCPMU) (Figure 1). These compounds were detected only in trace quantities (<0.01-0.03 ppm) in pulp and peels. No other dichloroaniline-containing metabolites were identified. The majority of radioactivity in the aqueous/organic fractions was characterized as polar unknowns.

The ^{14}C-containing residues that were identified in corn plants were: Following postemergence treatment, diuron was found at 13.2-95.2% of TRR (0.62-1.21 ppm) in whole plants, 4.1-13.1% of TRR (0.20-0.37 ppm) in foliage, and 57.1-70.4% of TRR (0.04-0.22 ppm) in cobs; very minor amounts of diuron were observed in kernels (2.4% of TRR, <0.01 ppm). Following preemergence treatment, diuron was detected at 22.0-48.4% of TRR (0.22-1.15 ppm) in whole plants and at 11% of TRR (0.35 ppm) in foliage; diuron was not detected in corn cobs or kernels. Other residues identified in corn matrices were DCPMU at 1.4-46.4% of TRR (<0.01-1.60 ppm) and DCPU at 2.1-50.0% of TRR (0.02-2.22 ppm) from both types of treatments. No other metabolites were identified. Polar unknowns accounting for 0.5-23.6% of TRR (0.01-1.44 ppm) in whole plants, foliage, cobs, and kernels from both treatments were observed.

The ^{14}C-containing residues that were identified in wheat were: diuron, at 34.2-98.5% TRR (0.12-80.79 ppm) in wheat forage harvested 0-71 days posttreatment, and at 11.2% TRR (0.002 ppm) and 5.2% TRR (0.051 ppm) in mature wheat grain and straw, respectively. The diuron metabolite DCPMU was identified at 7.7-25.6% TRR (0.002-0.24 ppm) in all wheat commodities except forage harvested on the day of treatment, and DCPU was identified at 1.2-34.5% TRR (0.02-1.01 ppm) in all wheat commodities except mature grain. No other metabolites were identified. Two polar unknowns accounting for 2.4-34.9% TRR (0.007-0.023 ppm) were detected in wheat forage harvested 71 days posttreatment and in mature grain and straw.



Diuron: 3-(3,4-dichlorophenyl)-1,1-dimethylurea

DCPMU; IN-15654: 3-(3,4-dichlorophenyl)-1-methylurea

DCPU; IN-R915: 3,4-dichlorophenylurea

Figure 1.

Livestock Commodities:

The ^{14}C-containing residues that were identified in lactating goats were: The principal residue identified was DCPU which comprised 10% of TRR in milk, 27% of TRR in fat, 35% of TRR in kidney, 23% of TRR in liver, and 22% of TRR in muscle. The parent and other dichloroaniline-containing metabolites (i.e., 3,4-DCA and DCPMU) were detected in trace quantities (#0.01 ppm each) except in liver (0.12 ppm). Four minor (each #6% of TRR) hydroxylated metabolites (2-OH-DCA; 2-OH-DCPU; 2-OH-DCPMU; and N-acetyl-2-OH-DCA) were also detected; these metabolites were not observed in plants and would not be determined by the enforcement method.

The major portion of radioactive residues in milk was comprised of several conjugated polar components which collectively accounted for 56% of TRR. These polar components also accounted for substantial portions of the total radioactivity in liver (collectively 25% of TRR) and kidney (collectively 23% of TRR). Attempts to further elucidate the nature of these polar materials using various techniques (e.g., enzyme digestions, heat treatment) were not successful.

Poultry:

The ^{14}C-containing residues that were identified in laying hens were: DCPU, which comprised ~45% of TRR in liver, ~67-75% of TRR in muscle, ~47% of TRR in skin with fat, ~57% of TRR in egg yolk, and ~54% of TRR in egg white. The parent, other dichloroaniline-containing metabolites (i.e., DCPMU), and hydroxylated metabolites (2-OH-diuron, 2-OH-DCA, 2-OH-DCPU, 2-OH-DCPMU, and N-acetyl-2-OH-DCA) were identified only in trace quantities (mostly at #0.01 ppm each).

Adequate radiovalidation data were submitted for the proposed enforcement method for animal commodities. The GC method recovered ~86 to >100% of the TRR in liver, kidney, and muscle; however, the method recovered only 10% of the TRR in milk and 25% of the TRR in fat. The low

recovery in milk was previously addressed (DP Barcodes D195058 and D195068, 11/30/93, R. Perfetti). It was concluded that because the major portion of radioactive residues in milk appear to be hydroxy metabolites which cannot be converted to DCA and do need not be quantitated, a new method would not be required for milk. Instead, it was determined that the levels of diuron residues in milk identified in the ruminant feeding study would be multiplied by 10 to account for all of the exposure in the risk assessment. The low recovery in fat was most likely due to the low residue levels present in fat. In a separate radiovalidation study, the GC method recovered -62 to 77% of the TRR in poultry liver and muscle, and 58 to 65% of the TRR in egg whites and yolks.

Dietary Water

The environmental data base is complete, diuron is persistent in the environment and has potential for leaching to ground and surface water. The metabolism studies of diuron in a variety of environmental conditions demonstrate that monochlorinated methylphenyl urea (MCMPU) and monochlorinated dimethylphenyl urea (MCDMPU) can be formed under some conditions and that MCDMPU is a major degredate in aquatic aeobic and anerobic studies. DCPMU was identified as a major degradate in several studies and 3,4- DCA, DCMU, PDMU were identified as minor metabolites.

The MARC raised concerns for MCPDMU based on an analogous compound, monuron. With the exception of the position of the chlorine, the structures are identical. There are cancer concerns for monuron but the target organs are different than those effected by diuron. The MARC recommended that a separate cancer assessment be conducted for MCPDMU..

MARC Decisions & Rationale

Plants: The MARC concluded that for tolerance expression and risk assessment purposes, the residues of concern in/on plants are diuron and its metabolites convertible to 3,4-dichloroaniline. This decision was based on the assumption that the metabolites DCPMU, and DCPU would not be any more or less toxic than the parent and in consideration of the analytical methods used to collect field trial data which are not capable of measuring each metabolite individually. 3,4-Dichloroaniline is not of toxicological concern for the endpoints regulated for diuron, but methods specific for diuron, DCPMU, and DCPU are not widely employed.

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Livestock Commodities:

The MARC concluded that for the tolerance expression and risk assessment purposes, the residues of concern in/on livestock and poultry are diuron and its metabolites convertible to 3, 4-dichloroaniline. This decision was based on the

assumption that the metabolites DCPMU and DCPU would not be any more or less toxic than the parent and in consideration the analytical methods used to collect field trial data which are not capable of measuring each metabolite individually. To account for the poor recovery of hydroxylated metabolites from milk, it was determined that the levels of diuron residues in milk identified in the ruminant feeding study would be multiplied by 10 to account for all of the exposure to diuron-related residues in the risk assessment.

Drinking Water: The MARC concluded that for risk assessment purposes, the residues of concern in drinking water are parent, DCPMU, and MCPDMU. Based on a structural analogy to monuron, the MARC recommended that a separate cancer assessment be conducted for MCPDMU.

cc: JSPunzi (RRB2), D.Locke (RRB2), Diuron Reg. Std. File, Diuron SF, RF, LAN.
RD/I: RRB2 Chem Review Team (07/11/2001), Alan Nielsen (08/31/2001), MARC Chair (07/11/2001).
John S. Punzi:7509C:RRB2:CM2:Rm 712M:703-305-7727:07/11/2001.